

CODING FORMS FOR SRC INDEXING

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Document Title	SUPPORT: T-7499 (PERFLUOROBUTYL SULFONYL FLUORIDE): ACUTE (FOUR-HOUR) INHALATION STUDY IN RATS, WITH COVER LETTER DATED 09/28/00		
Chemical Category	PERFLUOROBUTANESULFONYL FLUORIDE		

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OFFICE OF TOXIC SUBSTANCES
CODING FORM FOR GLOBAL INDEXING

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28 September 2000

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CERTIFIED MAIL

Document Processing Center (7407)
Attn: Section 8(e) Coordinator
Office of Toxic Substances
US Environmental Protection Agency
410 M Street, SW
Washington, DC 20460

Contain NO CBI

Re: TSCA 8(e) SUBSTANTIAL RISK NOTICE (SUPPLEMENTAL) ON:
Perfluorobutanesulfonyl Fluoride: CAS#375-72-4

Dear Sir:

3M has conducted an acute (four-hour) inhalation toxicity study in rats and determined that perfluorobutanesulfonyl fluoride causes signs of neurotoxicity. During and immediately after the inhalation exposure the rats showed the following signs: restless behavior, vocalization, jumping, and convulsions. The signs of neurotoxicity reversed soon after exposure. Neurotoxicity signs previously had been reported in another species, mice, in an acute inhalation study [TSCA 8(e) Substantial Risk Notice, dated 30 July 2000]. Post-exposure, the rats had body weight loss and reduced food consumption. The LC₅₀ (4-hour) was > 5,000 ppm. However, the signs of neurotoxicity were seen at lower concentrations of 1,000 and 5,000 ppm (see attached study summary from study report).

3M uses this chemical as a site limited intermediate with the following industrial hygiene practices: supplied air respiratory protection for potential exposure associated with charging operations, chemical protective clothing with charging and local exhaust ventilation.

Please contact Larry Zobel, Staff Vice President and Medical Director, 651-733-5181, for further information.

Sincerely,

Larry R. Zobel MD



BEHQ-99-14523

Larry R. Zobel, MD
Staff Vice President and Medical Director

MR 39961

bc: T. J. DiPasquale
K. E. Reed
G. L. Adams
W. A. Weppner



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T-7499

ACUTE (FOUR-HOUR) INHALATION STUDY IN RATS

Data requirement: US EPA OPPTS Guidelines No. 870.1300
Project identity: MIN 244
Study completed on: 15 September 2000

Sponsor

3M Medical Department,
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USA.

Research Laboratory

Huntingdon Life Sciences Ltd.,
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ENGLAND.

SUMMARY**Test substance**

A clear colourless liquid identified as T-7499 and estimated to contain 96 - 98% Perfluorobutyl sulfonyl fluoride.

Test animals

Albino rats (Sprague-Dawley in origin). One control group and 3 test groups, each of 5 male and 5 female rats.

Route of administration

By inhalation of a test atmosphere containing vapour generated from the test substance.

Duration of exposure

Groups 1 to 3 - Four-hour continuous snout-only exposure.

Group 4 - Terminated during equilibration period.

Observation period

Group 1 to 3 - Fourteen days post exposure.

Group 4 - Discarded on Day 7.

Exposure levels

Groups 2 and 3 - The time-weighted average chamber concentrations of T-7499 were 999 ppm and 5,054 ppm for Groups 2 and 3 respectively.

Group 4 - Exposure of Group 4 (Target 20,000 ppm) was not performed. During the equilibration period the nature and severity of the clinical signs observed justified immediate termination of exposure on humane grounds, in accordance with the UK Home Office guidelines. An atmosphere generation trial, without rats, conducted following cessation of the Group 4 exposure indicated that the chamber concentration of T-7499 was likely to have attained approximately 15,000 ppm before the exposure was stopped.

Mortality

A single Group 3 male rat was sacrificed for humane reasons, on Day 6 of the observation period, due to the deteriorating condition of an eye injury sustained during exposure.

Clinical signs**During exposure**

Groups 2 and 3 - Exaggerated breathing and a decreased breathing rate were evident in Group 3 rats from 30 minutes into exposure and in Group 2 rats from 30 minutes and 3 hours into exposure respectively.

Other clinical signs noted during exposure included initial restless behaviour followed by reduced motor activity, and sudden movements characterised by pronounced jumping. The onset of these signs occurred earlier during exposure of rats at the higher concentration (Group 3). As a consequence of the pronounced jumping, the snout/limbs of Group 3 rats were observed to protrude through the bars of the confinement cage, resulting on occasions in a trapped snout. Fine muscle tremors and vocalising were also noted for a Group 2 male and female respectively.

Group 4 - Clinical signs evident during the equilibration period included restless behaviour, vocalisation, convulsions and a pronounced jumping, resulting in protrusion of snout/limbs and entrapment of snouts through the bars of the confinement cage. Exposure of Group 4 rats was suspended during the equilibration period due to the nature and severity of these signs.

During the observation period - Exaggerated breathing was evident in all test rats immediately following exposure, persisting up to Days 1 and 2 for Groups 2 and 3 respectively. A slow breathing rate was also noted for Group 3 rats following exposure, persisting for at least 2 hours post exposure.

Additional clinical signs noted post exposure included the following: lethargy (all test groups); immobility (Groups 3 and 4); hyperactive when handled (a Group 2 female); sensitive to touch and vocalisation when handled (Groups 2 and 4); extremities cold to touch (Group 3); lacrimation (Group 3 females); yellow staining around uro-genital area (Group 2 and a Group 3 male); yellow substance on fur of snout/jaws (Group 3).

Clinical signs noted following exposure and considered associated with the pronounced jumping evident during exposure included the following: an apparent swelling under the left eye (a Group 2 male); left eye damaged and dark in colour (a Group 3 male); a cut to upper lip (a Group 4 male); apparent swelling of the muzzle (a Group 2 female).

Brown staining on whole body was noted for all Group 3 females on Days 1 and 2 of the observation period.

Rat 45M (Group 3) was sacrificed on Day 6, for humane reasons, due to the deterioration in the condition of an eye injury sustained during exposure. The left eye was damaged, dark in colour and swollen. A clear discharge from the eye was noted and the area around the eye was also swollen. These observations are considered consistent with infection of the eye, 6 days following injury.

There were no treatment-related findings for Groups 2 to 4 from Days 2, 3 and 1 of the observation period respectively.

Bodyweight

A mean bodyweight loss was evident for Groups 2 and 3 on Day 1 of the observation period and was marked for Group 3 male rats. A higher bodyweight gain was subsequently noted for Group 3 males on Day 2, compared with controls.

Food consumption

A reduction in food consumption was evident for Groups 2 and 3 on Day 1 and was marked for Group 3 males, persisting for approximately 5 days.

Water consumption

A reduction in water consumption was evident for Group 2 male rats and Group 3 rats on Day 1 and was marked for Group 3 rats.

Macroscopic pathology

External findings noted for the rat sacrificed for humane reasons included a damaged left eye. The eye and surrounding area were swollen and a clear discharge was noted from the eye.

Lung weights

There were no treatment-related effects.

Conclusion

The LC₅₀ (4-hour) of T-7499 was not determined for humane reasons, due to the nature and severity of the clinical signs evident during exposure of rats at concentrations in excess of approximately 5,000 ppm.